

ABSTRACT

THERAPEUTIC AND DIAGNOSTIC METHODS DEPENDENT ON CYP2A
ENZYMES

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A method of regulating the activity of human cytochrome P450 isozyme CYP2A6 to control nicotine metabolism or decrease the production of
10 carcinogens from procarcinogens, such as those present in tobacco smoke, in an individual by selectively inhibiting CYP2A6. Various prophylactic (i.e., prevention and treatment) compositions and methods are also described, including an improved oral nicotine composition and method comprising the use of nicotine together with an inhibitor of the CYP2A6 enzyme. Furthermore, it has been discovered that the
15 presence in an individual of a mutant allele of human cytochrome P450 enzyme CYP2A6 (referred to throughout this specification as "CYP2A6" for brevity) is predictive of an individual who: (1) has a decreased risk of becoming a smoker, (ii) will smoke less if he/she becomes dependent, and/or (iii) may be at relatively lower risk for cancer due to both decreased smoke exposure and decreased CYP2A6 –
20 mediated activation of tobacco smoke and other procarcinogenic substrates. This invention provides diagnostic methods for predicting tobacco dependence risk and risk for cancers related to CYP2A6 substrates in an individual by analyzing for the presence of a mutant genotype for human cytochrome P450 enzyme CYP2A6 in an individual, ranging from gene duplication (multiple copies of CYP2A6) to single or
25 even no copies due to null alleles or gene deletion.